

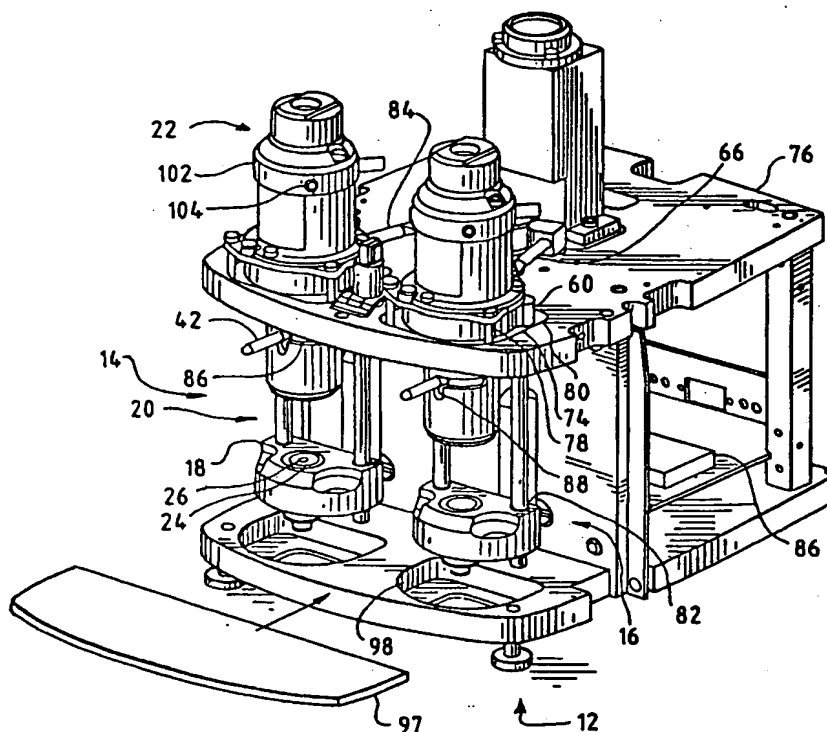


INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification ⁷ : G01N 33/49, 11/16		A1	(11) International Publication Number: WO 00/49402
			(43) International Publication Date: 24 August 2000 (24.08.00)
(21) International Application Number: PCT/US00/04538		(81) Designated States: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, ARIPO patent (GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).	
(22) International Filing Date: 22 February 2000 (22.02.00)			
(30) Priority Data: 09/255,099 22 February 1999 (22.02.99) US			
(71) Applicant: HAEMOSCOPE CORPORATION [US/US]; 7855 Gross Point Road, Suite G-4, Skokie, IL 60077 (US).			
(72) Inventors: COHEN, Eli; 3651 Grove Avenue, Skokie, IL 60076 (US). DELMENICO, Peter, R.; 1321 Oak Avenue, Apartment 2B, Evanston, IL 60201 (US). RAVIN, Gabriel; 1048 Woodlawn Road, Glenview, IL 60025 (US). GEORGE, William, R.; 1227 Laurel Street, Santa Cruz, CA 95060 (US). LAKE, John, A.; 925 Forest Avenue, Apartment 1E, Evanston, IL 60202 (US).			
(74) Agent: READ, David, C.; Marshall, O'Toole, Gerstein, Murray & Borun, 6300 Sears Tower, 233 South Wacker Drive, Chicago, IL 60606-6402 (US).			

Published*With international search report.**Before the expiration of the time limit for amending the claims and to be republished in the event of the receipt of amendments.***(54) Title: METHOD AND APPARATUS FOR MEASURING HEMOSTASIS****(57) Abstract**

A method and apparatus are provided for measuring hemostasis, the apparatus includes a torque sensing column having a torque sensing element and a drive ring disposed around a body of the column and in registration with the column so as to allow rotation of the drive ring around a longitudinal axis of the column. The apparatus further includes a first guide shaft rigidly secured to the drive ring, the guide shaft extending parallel to the longitudinal axis of the column and a cup holder movably attached to the guide shaft, allowing the cup holder to move parallel to the longitudinal axis of the column. The apparatus also includes a sample cup adapted to engage the cup holder on an outer surface and the torque sensing element of the torque sensing column on an inner surface.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece	ML	Mali	TR	Turkey
BG	Bulgaria	HU	Hungary	MN	Mongolia	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MR	Mauritania	UA	Ukraine
BR	Brazil	IL	Israel	MW	Malawi	UG	Uganda
BY	Belarus	IS	Iceland	MX	Mexico	US	United States of America
CA	Canada	IT	Italy	NE	Niger	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NL	Netherlands	VN	Viet Nam
CG	Congo	KE	Kenya	NO	Norway	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NZ	New Zealand	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	PL	Poland		
CM	Cameroon	KR	Republic of Korea	PT	Portugal		
CN	China	KZ	Kazakhstan	RO	Romania		
CU	Cuba	LC	Saint Lucia	RU	Russian Federation		
CZ	Czech Republic	LI	Liechtenstein	SD	Sudan		
DE	Germany	LK	Sri Lanka	SE	Sweden		
DK	Denmark	LR	Liberia	SG	Singapore		
EE	Estonia						

METHOD AND APPARATUS FOR MEASURING HEMOSTASIS

Field of the Invention

5 The field of the invention relates to testing of blood samples and more particularly to devices for testing hemostasis.

Background of the Invention

10 Methods of measuring the coagulation characteristics of blood are known. Some such devices attempt to simulate the natural flow of blood in the veins and arteries of a living subject.

 An accurate measurement of the ability of a
15 patient's blood to coagulate in a timely and effective fashion is crucial to certain surgical and medical procedures. Accelerated (rapid) and accurate detection of abnormal coagulations is also of particular importance with respect to appropriate treatment to be
20 given to patients suffering from clotting disorders. Often the condition of such patients makes it necessary to administer anti-coagulants, certain fibrinolytic agents, anti-platelet agents, or blood components in a quantity which may only be determined after taking into
25 account the abnormal components or "factors" of the patient's blood which may be contributing to the clotting disorder.

 One measure of blood clotting is provided by the Thromelastograph (TEG®) Coagulation Analyzer
30 manufactured by Haemoscope of Skokie, Illinois. The Haemoscope device measures the mechanical properties of the clot throughout its structural development.

A number of references describe instruments for measuring blood clotting characteristics based upon simple mechanical movements. These instruments monitor the elastic properties of blood as it is induced to
5 clot under a low shear environment resembling sluggish venous blood flow. The patterns of change in shear elasticity enable the determination of the kinetics of clot formation, as well as the strength and stability of the formed clot. The strength and stability of the
10 clot provide information about the ability of the clot to perform the "work of hemostasis" (i.e., stop or prevent abnormal bleeding) and about the adequacy of blood platelet-fibrin interaction. The kinetics of clot formation provide information about coagulation
15 factors available for clot formation. Analysis of the information provides results which are useful to predict bleeding, to monitor and manage thrombosis, and to monitor fibrinolysis.

While the instrument of the reference is effective
20 in measuring hemostasis based upon resistance to mechanical movement, the apparatus necessary to cause movement and torque measurement is unnecessarily complex. The apparatus is even more difficult to load and unload. Because of the importance of measuring
25 blood clotting, a better apparatus for measuring hemostasis is needed.

Summary

A method and apparatus are provided for measuring
30 hemostasis. In one embodiment, the apparatus includes a torque sensing column having a torque sensing element and a drive ring disposed around a body of the column

and in registration with the column so as to allow rotation of the drive ring around a longitudinal axis of the column. The embodiment further includes a first guide shaft rigidly secured to the drive ring, the
5 guide shaft extending parallel to the longitudinal axis of the column and a cup holder movably attached to the guide shaft, allowing the cup holder to move parallel to the longitudinal axis of the column. The embodiment also includes a sample cup assembly adapted to engage
10 the cup holder on an outer surface and the torque sensing element of the torque sensing column on an inner surface.

The apparatus includes novel features which allow for the quick and easy replacement of blood samples. A
15 unobstructed front surface of the apparatus allows the operator better access for easier cup and blood sample placement. A control lever on a torque measuring column of the apparatus allows a pin of the sample cup
20 assembly to be quickly and easily ejected. The sample cup holder may be lifted to a convenient position and a button on the bottom of the holder activated to release the sample cup assembly for easy removal.

Brief Description of the Drawings

25 FIG. 1 depicts an embodiment of a system for measuring hemostasis in accordance with the invention;

FIG. 2 depicts an embodiment of a measuring unit for use with the system of FIG. 1;

30 FIG. 3 depicts an embodiment of a torque measuring column for use with the measuring unit of FIG. 2;

FIG. 4 depicts an example of a sample cup carrier for use with the measuring unit of FIG. 2;

FIG. 5 depicts a cut-away side view of the cup carrier of FIG. 4;

FIG. 6 depicts an example of a drive mechanism of the measuring unit of FIG. 2;

5 FIG. 7 depicts a side view of a mounting feature of a torque measuring column of the system of FIG. 1;

FIG. 8 depicts an alignment fixture that may be used with the system of FIG. 1; and

10 FIG. 9 depicts a top view of a torque measuring pin of the system of FIG. 1.

Detailed Description

FIG. 1 is a block diagram of a system 10 for measuring hemostasis, generally, in accordance with an
15 illustrated embodiment of the invention. Included within the system 10 is a measuring unit 12 and data collection unit 14 (e.g., a personal computer (PC), datalogger, etc.). The system 10 is constructed in a modular form. Features discussed below provide for the
20 quick and easy replacement of individual modules of the system 10 without the need for re-calibration or complex re-alignment steps.

Under the illustrated embodiment, hemostasis may be measured by the system 10 in terms of a series of
25 shear elasticity measurements (e.g., in terms of dyn/cm^2). The resulting hemostasis profile may be used as a measure of the time it takes for the first fibrin strand to be formed, the kinetics of clot formation, the strength of the clot (in shear elasticity units of
30 dyn/cm^2) and dissolution of the clot.

In general, the system 10 measures a clot's physical properties by the use of a combination

cylindrical cup and matching shear-inducing pin. The combination cup and matching pin may be constructed generally as taught by U.S. Patent No. 5,223,227 to Zuckerman, assigned to the assignee of the present invention and incorporated herein by reference.

FIG. 2 is a perspective view of one example of the measuring unit 12. Included within the measuring unit 12 may be a first and a second measuring station 14, 16. While the system 10 shows two stations, 14, 16, it should be understood that there is no practical limit of the number of test stations that may be incorporated into the system 10. The measuring stations 14, 16 may be functionally identical and facilitate the processing of two separate blood samples at the same time.

An explanation will now be provided of the operation of the first measuring station 14. For purposes of explanation, it may be assumed that the structure of the second station 16 is substantially identical to first station 14.

Each measuring station 14, 16 may include at least three main structures. The stations 14, 16 may include a cup carrier 18, a cup carrier drive system 20 and a torque measuring column 22.

The cup carrier 18 may be provided with a receptacle sized to accept a sample cup 24 (containing a blood sample). Once a sample cup 24 is inserted into the cup carrier 18, a pin 26 may be inserted into the cup 24 of the cup carrier 18. The sample cup 24 and pin 26 may be fabricated of an inexpensive material (e.g., plastic) intended for a one-time use.

One difference between the cup and matching pin of the Zuckerman '227 patent over that used herein relates

to a configuration of the pin. Under the embodiment, the torque sensing pin 26 (FIG. 9) is provided with a fully enclosing upper flange 114 which functions to completely close an upper opening of the sample cup 24. Such closure has been found important in preserving the integrity of the blood sample against the effects of drying and oxidation.

The pin 26 is also provided with a circular aperture 116. The circular aperture reduces the difficulty in engaging the pin 26 with the torque measuring column 22 as explained in more detail below.

Once the sample cup 24 and pin 26 is inserted into the cup carrier 18, the carrier 18 may be manually lifted into contact with a bottom of the torque measuring column 22. Once the carrier 18 makes contact with the bottom of the measuring column 22, a skewer 28 (see cross-sectional view of the column 22 in FIG. 3) engages the circular center hole of the pin 26.

FIG. 4 is a cut-away view of an embodiment of the cup carrier 18. Shown included within the cup carrier 18 is a sample cup 24 and pin 26. Shown between the cup 24 and pin 26 is a blood sample 30.

The cup 24 may be fabricated for any convenient size blood sample (e.g., 360 μ L) consistent with sampling accuracy. An outer diameter of the pin 26 and inner diameter of the cup 24 may be selected to provide a 1mm gap on each side (2 mm total) within which the blood sample resides.

During testing, the cup holder 18 is oscillated (i.e., rotated) around the longitudinal axis of the skewer 28. For example, the cup holder 18 may be rotated to a distance of 2.4 degrees on either side of

a center point during each cycle (4.83 degrees of total travel). Each cycle may last 10 seconds with a 1½ second rest period at each end of the excursion.

During rotation of the cup holder 18 and cup 24,
5 the relative movement of the cup 24 and stationary position of the pin 26 creates a shear action between the inner surface of the cup 24 and outer surface of the pin 26. The shearing action causes a shear movement among adjacent blood molecules lying between,
10 resulting in coagulation.

As the blood coagulates, the shear resistance between adjacent molecules in the blood sample increases and the shear force that may be transmitted from the cup 24 to the pin 26 increases. By measuring
15 the torque imparted to the skewer 28 through the blood 30, a thrombo-elastic graph may be created over a time period.

In order to preserve the integrity of the blood testing process, a port 93 (FIG. 3) is provided through
20 the torque measuring column 22 for introducing a protective oil over the blood sample 30. The port 93 is angled for the insertion of a pipette into the junction area between the pin 26 and cup 24.

By introducing the oil into the area of the
25 junction, capillary action causes the oil to be drawn into the cup 24 and overlay and protect the blood 30. Protection of the blood 30 has been found to be an important feature (against drying of the blood) where extended periods are required for coagulation testing.

30 As a further feature for protection of the blood sample 30, a relatively closed cavity 38 is provided at the lower end of each torque measuring column 22. The

closed cavity functions to provide a protected environment for the blood sample during testing. Such closed cavity 38 not only reduces the possibility that airborne contaminants may enter the sample 30, but also
5 tends to control humidity of the environment surrounding the cup 24.

Returning now to the illustrative example of FIG. 3, it may be seen that the skewer 28 is coupled to a torque transmission shaft 32 which freely floats within
10 the column 22 during test conditions, suspended from a tungsten wire 34. The tungsten wire 34 provides a progressive resistance to torque from the skewer 28.

The tungsten wire, in turn, is supported by a stationary cross-bar 31 disposed in a V-groove. The V-
15 groove provides a vertical reference point for alignment of the pin 26 and cup 24.

An appropriate non-contacting rotation detector (e.g., rotary variable differential transformer (RVTD), rotary variable inductive transformer (RVIT),
20 laser/mirror/CCD arrangement, etc.) 36 may be provided to detect rotation of the transmission shaft 32 (and skewer 28) caused by torque transmitted by the shear force through the blood to the pin 26. By multiplying a detected rotation of the shaft by a spring constant
25 of the tungsten wire 34, a torque value may be periodically determined and transmitted to the data collection unit 14 through the interconnecting cable 16.

The tungsten wire 34 may be fabricated to any
30 appropriate diameter (e.g., 0.007 inch) and length (e.g., 2 inches) consistent with an expected torque measuring range. Further, the column 22 is fabricated

for easy replacement of the wire 34 (or the column 22 itself) where it becomes necessary (for research or other purposes) to adjust a torque measuring range. This also greatly simplifies replacement of torsion
5 wires damaged by misuse or otherwise.

The simplified procedure for replacing the torsion wire greatly increases the flexibility and utility of the system 10. For example, the easily replaceable torsion wire allows a weaker torsion wire (for
10 increased sensitivity) to be used for measuring weaker clots, or a stronger torsion wire for stronger clots.

To replace a wire 34, the user moves the control lever 42 to a locked position. Next, the set screw 35 (FIG. 3) is loosened to release the wire 34.

15 To remove the wire 34, a screw-on cap 33 is removed and a pair of needle-nose pliers (not shown) may be used to grasp an end 31 of the wire 34 and lift it out of the column 22. A replacement wire 34 may be inserted in place of the removed wire 34.

20 Once the replacement wire 34 is inserted, the set screw 35 may again be tightened. Once the set screw is tightened, the skewer 28 may be centered using centering screws 102, 104 (FIG. 1). Adjustment of the centering screws 102, 104 allows a support cap 106
25 (FIG. 3) to be laterally adjusted to center the skewer 28 over the cup 24.

To center the skewer 28 a fixture 110 (FIG. 8) may be inserted in place of the cup 24 into the cup holder 18. A spacer block (not shown) may be used to bring
30 the skewer 28 into vertical proximity with a reference point 112 of the fixture 110. The centering screws 102, 104 may be adjusted as necessary to center the

skewer 28 over the reference point 112 of the fixture 110.

To complete installation of the new wire 34, a torque constant (i.e., measured in torque units per
5 degree of deflection) may be entered through the keyboard 15 into the CPU 14. Alternatively, a lookup table of torque constants may be provided within the CPU 14 and accessed via a part number of a wire 34 entered through the keyboard. The torque value may be
10 used to determine a measured torque by multiplying a torque deflection (in degrees) by the torque constant.

Turning now to loading of the cup carrier 18, a side cut-away view is shown in FIG. 5 of the cup carrier 18. A cavity 50 is provided in an upper
15 surface of the cup carrier 18 to receive the sample cup 24. Once the cup 24 and tip 26 are placed in the cavity 50, the cup carrier is lifted into contact with the bottom of the column 22 of FIG. 3. Once in contact a spring-loaded button 52 provided on the bottom of the
20 cup carrier 18 is activated to seat the tip 26 onto the skewer 28. As the button 52 is activated, an inner hole of the tip 26 is urged onto the skewer 28 up over a shoulder 40 on the skewer 28 within a cavity 38 located in the bottom of the column 22.

25 Once the tip 26 is seated on the skewer 28, the cup carrier 18 may be lowered and the cup 24 seated back into its own respective cavity 50. After the cup 24 is seated, the cup 24 may be filled with a blood sample 30 and again raised into an operating position
30 against the bottom of the column 22. The cup 24 may be raised and lowered slightly several times, thereby using the pin 26 to mix the sample prior to testing.

Once the carrier 18 has been seated against the column 22, a registration lever 42 (FIG. 2) may be rotated to the right along a slot 86 to a test position. Moving the lever 42 to a test position
5 brings the tip 26 into a proper position with respect to the cup 24. Rotating the lever 42 to the right rotates a cam 44 which lowers the torque transmission shaft 32 from a locked position by a sufficient distance (e.g., 0.035 inch) to bring the tip 26 and cup
10 into a proper spatial alignment with the cup 24.

Once the cup 24 and tip 26 are brought into a proper relationship, an operator (not shown) may enter a patient name through a keyboard 15 on the data recorder 14. At the same time the drive mechanism 20
15 may be activated and testing may begin.

A detached partial perspective view of an illustrative embodiment of the drive system 20 is shown in FIG. 6. While the partial view of FIG. 6 shows the drive system 20 for the right testing station 16, it
20 may be assumed that the drive system for the left testing station 14 would be substantially identical (with the exception of the cam follower 68 facing the other direction).

Included within the drive system is a drive ring
25 60. A pair of parallel guide shafts 62, 64 extend downwardly from the drive ring 60. A positioning rod 66 extends radially outwardly from the drive ring 60 and engages a geared drive motor 72 through a cam follower 68 and cam 70.

30 The drive ring 60 circumferentially engages the column 22 around a first abutting surface 46 (FIG. 3). The column 22 maintains the drive ring 60 in a radial

alignment with the column 22 by moveable registration of an inner surface of the drive ring 60 against the first abutting surface 46.

Longitudinal alignment of the drive ring 60 with
5 the column 22 is maintained by trapping the drive ring 60 between a second abutting surface 48 (FIG. 3) and a mating surface 74 on a top plate 76 of the measuring unit 12. The column 22 is retained in a fixed relationship with the top plate 76 through the use of a
10 stepped hole 81 (FIG. 7). An outer diameter 49 (FIG. 3) of the column 22 is sized to engage the hole 81 of a slightly larger diameter 79 (e.g., 0.005-0.010 inch). A step 77 at the bottom of the hole 81 allows for a fixed spacing between the second abutting surface 48
15 and top plate 76 and free rotation of the drive ring 60.

A set of three screws 78 may be used to secure the column 22 to the top plate 76. Removal of the screws 78 also allows for the simple replacement of the torque
20 measuring column 22 should the need arise.

The set of guide shafts 62, 64 extend downwardly from the guide ring 60 through a set of slots 80 in the top plate 76 to engage the cup carrier 18. A set of linear bearings 82 on each carrier 18 allow the carrier
25 18 to be easily moved up or down the guide shafts 62, 64. A set of spring loaded clips 19 (FIG. 4) are provided below each linear bearing 82 to maintain the carrier 19 in a selected position during testing and otherwise.

30 Movement of the guide ring 60 is accomplished by operation of the positioning rod 66. The cam follower 68 of the positioning rod 66 is maintained in contact

with the cam 70 by operation of a spring 84. More specifically, a clockwise motion of the ring 60 (when viewed from above) is caused by the cam. A counterclockwise motion of the ring 60 is caused by the spring 84.

To obtain an appropriate cycling rate, the motor 72 may be geared to obtain a speed of one revolution every 10 seconds. A flat spot may be provided on the cam 70 at a high point and low point to allow for a one and one-half second pause at the end of each direction of travel. The profile of the cam 70 may be changed as needed to provide a wide range of periodic motions.

The CPU 14 may provide for any number of test intervals. For example, a standard test interval of 10-15 minutes may be used. Alternatively, the test may be extended to 2-3 hours for research purposes.

To maintain the blood sample 30 at an optimal temperature (e.g., $98.6^{\circ}\text{F} \pm 0.1^{\circ}\text{F}$) for testing, a heater 54 and temperature sensor 55 (e.g., RTD, thermocouple, etc.) (FIG. 5) are provided within each carrier 18. The temperature sensors 55 are disposed directly against the receptacle holding the cup 24. A flexible cable 56 may be used to connect and control the heater 54 through operation of a temperature controller 86 located within the sampling unit 12.

A dual channel temperature controller (e.g., a Love Controls Model 32A022-9502) may be used to provide separate temperature control and set points for each carrier 18. The use of separate temperature sensors 55 and close proximity to the blood sample 30 ensures that each blood sample 30 is maintained at a precisely controlled temperature. The availability of separate

set points on the controller 86 for each carrier provides the versatility of performing standard testing or testing under abnormal conditions.

Once a cup 24 and pin 26 have been installed into the system 10 (as described above), a blood sample 30 may be directed into the cup 24 using a pipette (not shown). The cup 24 may be raised and lowered against the pin 26 to mix the blood. The hemostasis profile may be obtained as described above.

Once testing is complete, the sample cup assembly 24, 26 may be easily removed by a series of quickly executed steps. The tip 26 may be ejected from the skewer 28 by moving the lever 42 to a load position (as shown in FIG. 2). The lever 42 may then be simply moved downward into a second slot 88 to eject the tip 26. Moving the lever 42 downward causes a center ring 94 to move downward based upon its distance from a pivot point 91. As the center ring 94 moves down it presses against a collar 92, which acts against a spring 96 to eject the tip 26.

Once the tip 26 has been ejected, the carrier 18 may be moved to a lower position and the cup 24 and tip 26 removed. The cup 24 and tip 26 may be ejected from the carrier 18 by lowering the carrier 18 until the button 52 on the bottom of the carrier 18 makes contact with a lower cover 97.

With a first hand, an operator may eject the pin 26. At the same time, the operator may begin moving the cup carrier 18 downward with her other hand. As the carrier 18 is moved downward, the cover 97 activates the button 52, lifting the cup assembly. As the button 52 is activated, the operator may remove the

cup assembly and replace it with another cup assembly. The sequence of steps may be performed as part of a single rapid sequence of steps without fear of spilling or compromising the integrity of the testing procedure.

5 Once the cup 24 and tip 26 have been removed, the carrier 18 may also be removed for cleaning and sterilization. To accomplish removal, the cover 97 is first removed. Under the cover 97, a cavity 98 is provided below the ends of the guide shafts 62, 64.

10 The cavities 98 allow the carrier 18 to be easily slid off the ends of the guide shafts 62, 64. Once detached from the guide shafts 62, 64, the carrier 18 may be slid forward and out of the measuring unit 12.

15 The simple and rugged construction of the test unit 12 allows for reliable and accurate testing of blood samples. The easy removal and disposal of sample cups and tips reduces the possibility of contamination or infection by users. The easy removal and cleaning of related parts further improves upon the overall ease
20 of use of the measuring unit.

Specific embodiments of a method and apparatus for measuring hemostasis according to the present invention have been described for the purpose of illustrating the manner in which the invention is made and used. It
25 should be understood that the implementation of other variations and modifications of the invention and its various aspects will be apparent to one skilled in the art, and that the invention is not limited by the specific embodiments described. Therefore, it is
30 contemplated to cover the present invention and any and all modifications, variations, or equivalents that fall

within the true spirit and scope of the basic
underlying principles disclosed and claimed herein.

Claims

1. Apparatus for measuring hemostasis, such apparatus comprising:

5 a torque sensing column having a torque sensing element;

a drive ring disposed around a body of the column and in registration with the column so as to allow rotation of the drive ring around a longitudinal axis of the column;

10 a first guide shaft rigidly secured to the drive ring, the guide shaft extending parallel to the longitudinal axis of the column;

a cup holder movably attached to the guide shaft, allowing the cup holder to move parallel to the
15 longitudinal axis of the column; and

a sample cup assembly adapted to engage the cup holder on a outer surface and the torque sensing element of the torque sensing column on an inner surface.

20

2. The apparatus for measuring hemostasis as in claim 1 wherein the drive ring further comprises a positioning rod extending radially outward from the drive ring.

25

3. The apparatus for measuring hemostasis as in claim 2 wherein the positioning rod further comprises a cam follower disposed on an distal end of the positioning rod.

30

4. The apparatus for measuring hemostasis as in claim 3 further comprising a drive motor with a drive shaft

of the drive motor lying parallel to the longitudinal axis of the torque sensing column.

- 5 5. The apparatus for measuring hemostasis as in claim 4 further comprising a cam disposed on the drive shaft of the motor and engaging the cam follower of the cam follower.
- 10 6. The apparatus for measuring hemostasis as in claim 5 further comprising a spring adapted to bias the cam follower against the cam.
- 15 7. The apparatus for measuring hemostasis as in claim 1 further comprising a linear bearing disposed in the cup holder for engaging and registering the cup holder to the first guide shaft.
- 20 8. The apparatus for measuring hemostasis as in claim 7 further comprising a second guide shaft rigidly secured to the drive ring, the second guide shaft extending parallel to the first guide shaft and moveably engaging the cup holder so as to maintain a fixed relationship between the cup holder and the longitudinal axis of the torque sensing column.
- 25 9. The apparatus for measuring hemostasis as in claim 1 further comprising a heater disposed in the cup holder and adapted to warm the sample cup.
- 30 10. The apparatus for measuring hemostasis as in claim 1 further comprising a torque pin engaging the sample

cup at a first end and engaging the torque sensing element at a second end.

11. Apparatus for measuring hemostasis, such apparatus
5 comprising:

means for containing a blood sample;
means for causing a relative shear motion among adjacent molecules of the blood sample;
means for detecting a torque between the means for
10 containing and the means for causing shear motion;
means circumferentially disposed around the means for detecting for imparting relative motion between the means for containing and means for causing shear motion.

- 15
12. The apparatus for measuring hemostasis as in claim 11 wherein the means for imparting relative motion further comprising means for imparting a reciprocating rotational motion.

- 20
13. The apparatus for measuring hemostasis as in claim 11 further comprising means for coupling the means for imparting motion to the means for containing.

- 25
14. The apparatus for measuring hemostasis as in claim 11 further comprising means for securing an outer housing of the means for detecting in a stationary position.

- 30
15. The apparatus for measuring hemostasis as in claim 11 further comprising means secured in a stationary

position for imparting a linear motion to the means for imparting relative motion.

16. The apparatus for measuring hemostasis as in claim
5 15 further comprising means for coupling the means for imparting linear motion to the means for imparting relative motion.

17. The apparatus for measuring hemostasis as in claim
10 11 further comprising means disposed within the means for containing for warming the blood sample.

18. The apparatus for measuring hemostasis as in claim
15 11 further comprising means for separating the means for containing from the means for causing shear motion.

19. The apparatus for measuring hemostasis as in claim
20 11 further comprising means for coupling the means for causing shear to the means for detecting torque.

20. The apparatus for measuring hemostasis as in claim
19 further comprising means for ejecting the means for causing shear from the means for coupling.

25 21. The apparatus for measuring hemostasis as in claim 11 further comprising means for replacing a torque wire.

22. The apparatus for measuring hemostasis as in claim
30 11 further comprising means for replacing a torque column without recalibration.

23. The apparatus for measuring hemostasis as in claim 11 further comprising means for controlling a testing environment of the blood sample.
- 5 24. The apparatus for measuring hemostasis as in claim 23 wherein the means for controlling the testing environment further comprises a fully enclosing upper flange on a torque sensing pin.
- 10 25. The apparatus for measuring hemostasis as in claim 23 wherein the means for controlling the testing environment further comprises a cavity in a lower end of a torque sensing column adapted to be closed by an upper surface of a sample cup holder.
- 15 26. A method of measuring hemostasis, such method comprising the steps of:
- placing a blood sample in a sample cup;
 - disposing a shear-inducing pin in the blood
 - 20 sample;
 - holding the shear-inducing pin stationary by coupling the tip to a torque sensing element of a torque measuring column;
 - securing the sample cup to a drive ring disposed
 - 25 circumferentially around the torque measuring column; and
 - reciprocally rotating the drive ring.
27. The method of measuring hemostasis as in claim 26
- 30 wherein the step of reciprocally rotating the drive ring further comprises rotating the drive ring through an arc of approximately 4.8 degrees.

28. The method of measuring hemostasis as in claim 26
wherein the step of reciprocally rotating the drive
ring further comprises coupling the drive ring to a
5 cam.

29. The method of measuring hemostasis as in claim 26
wherein the step of coupling the drive ring to a cam
further comprises radially disposing a position control
10 member of a periphery of the drive ring.

1/3

FIG. 1

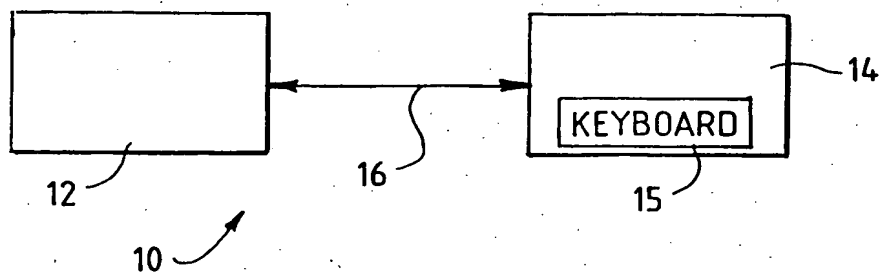


FIG. 2

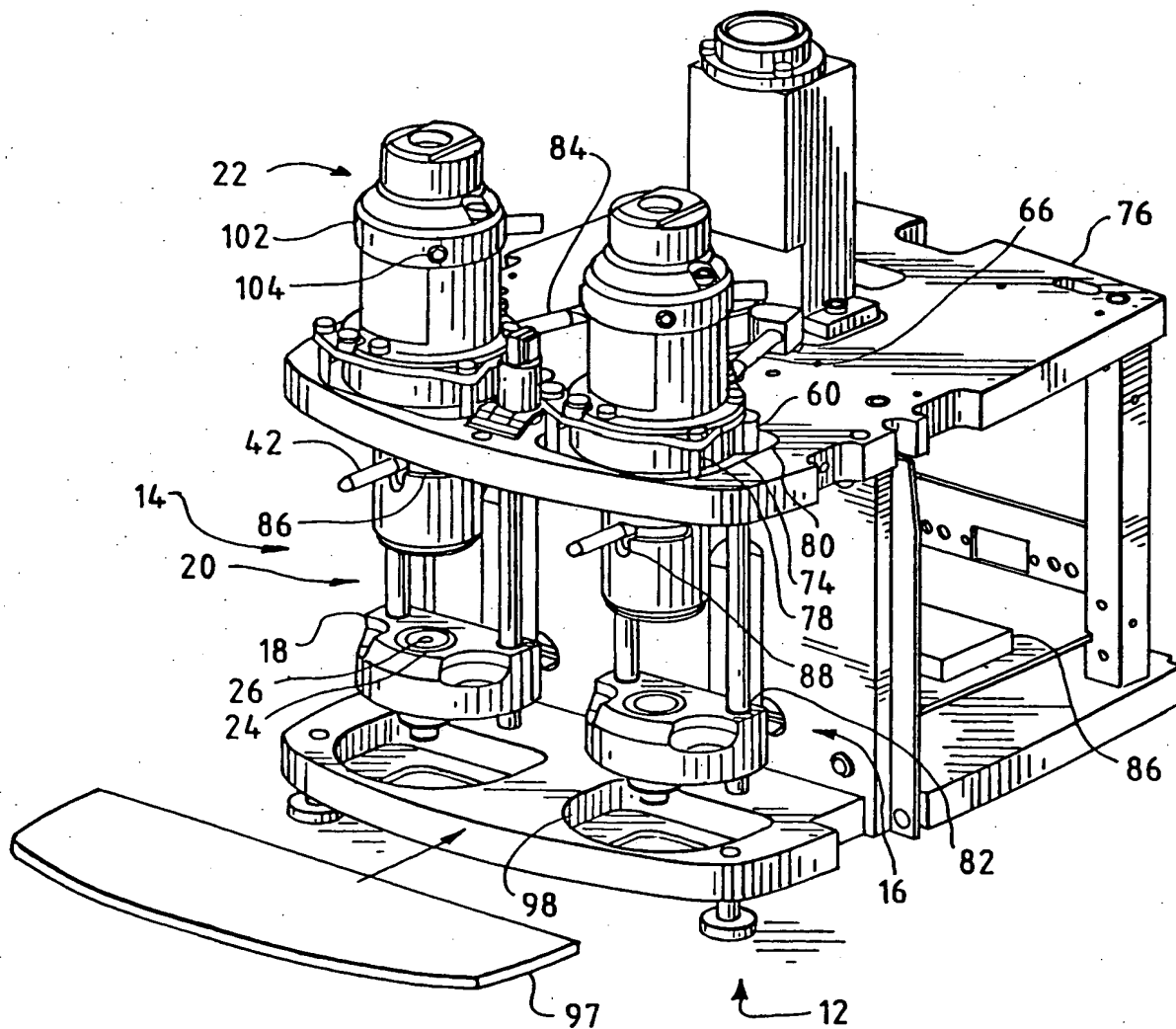


FIG. 3

2/3

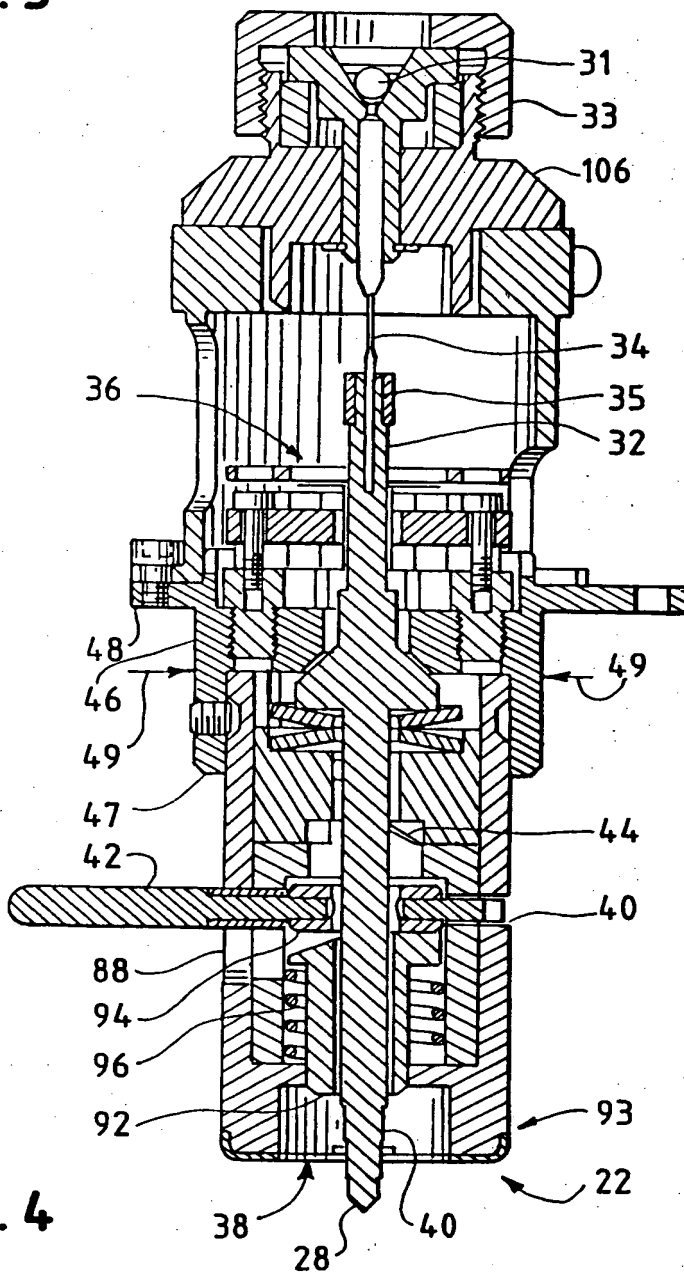


FIG. 4

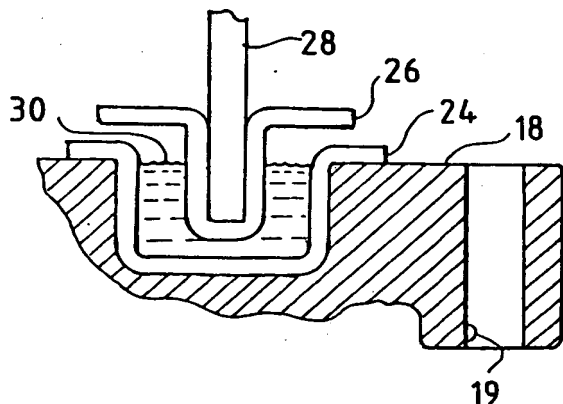
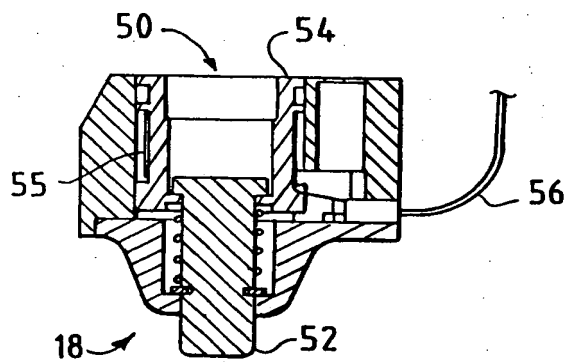


FIG. 5



SUBSTITUTE SHEET (RULE 26)

3/3

FIG. 6

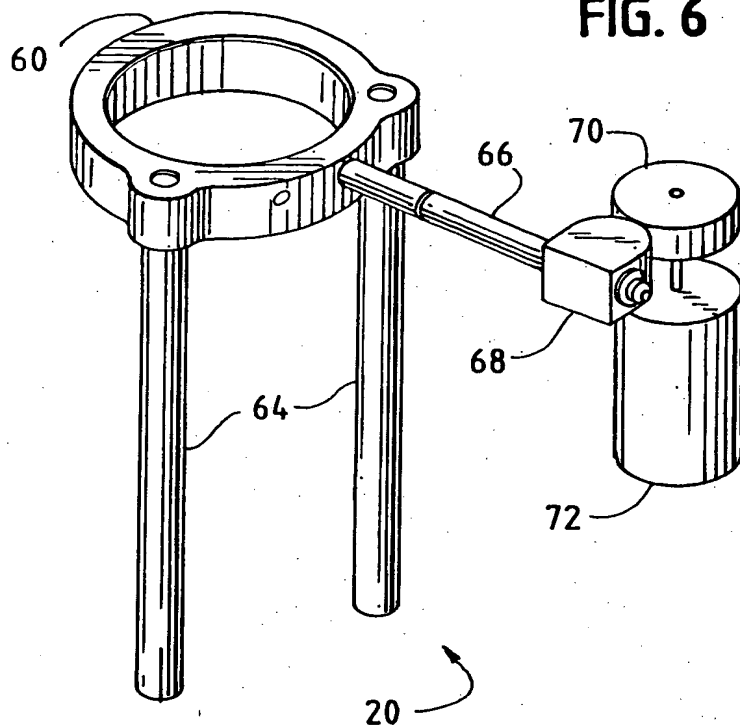


FIG. 7

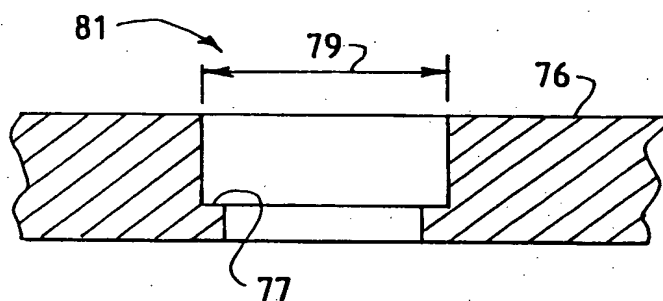


FIG. 8

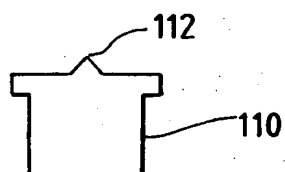
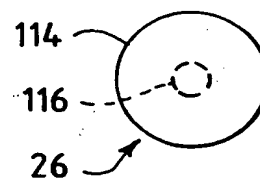


FIG. 9



SUBSTITUTE SHEET (RULE 26)

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/04538

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01N33/49 G01N11/16

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 G01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 2 004 376 A (FRESENIUS EDUARD DR) 28 March 1979 (1979-03-28) figure 1 page 1, line 54 - line 96	11-14
A	-----	1, 26
A	EP 0 404 456 A (HAEMOSCOPE CORP) 27 December 1990 (1990-12-27) cited in the application figures	1, 11, 26
A	----- EP 0 018 905 A (PROBIO DMS) 12 November 1980 (1980-11-12) figure 2 page 3, line 26 -page 7, line 3 ----- -/--	1, 11, 26

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search

15 June 2000

Date of mailing of the international search report

26/06/2000

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Colvin, G

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/04538

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>US 4 193 293 A (CAVALLARI FRANCESCO) 18 March 1980 (1980-03-18) figure</p> <p>-----</p>	1,11,26

INTERNATIONAL SEARCH REPORT

Information on patent family members

In .ational Application No

PCT/US 00/04538

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 2004376 A	28-03-1979	DE 2741060 A	22-03-1979
		FR 2402874 A	06-04-1979
		IT 1160642 B	11-03-1987
		JP 1377976 C	08-05-1987
		JP 54051891 A	24-04-1979
		JP 61045781 B	09-10-1986
		SE 7809602 A	14-03-1979
		US 4312217 A	26-01-1982
		US 4202204 A	13-05-1980
EP 0404456 A	27-12-1990	CA 2018788 A	19-12-1990
		JP 3031764 A	12-02-1991
		US 5223227 A	29-06-1993
EP 0018905 A	12-11-1980	FR 2455273 A	21-11-1980
		DE 3062173 D	07-04-1983
		ES 490923 D	16-02-1981
		ES 8102676 A	16-04-1981
		US 4328701 A	11-05-1982
US 4193293 A	18-03-1980	IT 1076740 B	27-04-1985
		DE 2740932 A	09-11-1978
		ES 469836 A	16-01-1979
		FR 2389137 A	24-11-1978